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A phase 1-2 clinical trial of gene therapy for recurrent glioblastoma multiforme by tumor transduction with the herpes simplex thymidine kinase gene followed by ganciclovir. GLI328 European-Canadian Study Group.

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This study has investigated the effects of herpes simplex thymidine kinase gene (HSV-tk) transfer followed by ganciclovir treatment as adjuvant gene therapy to surgical resection in patients with recurrent glioblastoma multiforme (GBM). The study was open and single-arm, and aimed at assessing the feasibility and safety of the technique and indications of antitumor activity. In 48 patients a suspension of retroviral vector-producing cells (VPCs) was administered by intracerebral injection immediately after tumor resection. Intravenous ganciclovir was infused daily 14 to 27 days after surgery. Patients were monitored for adverse events and for life by regular biosafety assaying. Tumor changes were monitored by magnetic resonance imaging (MRI). Reflux during injection was a frequent occurrence but serious adverse events during the treatment period (days 1-27) were few and of a nature not unexpected in this population. One patient experienced transient neurological disorders associated with postganciclovir MRI enhancement. There was no evidence of replication-competent retrovirus in peripheral blood leukocytes or in tissue samples of reresection or autopsy. Vector DNA was shown in the leukocytes of some patients but not in autopsy gonadal samples. The median survival time was 8.6 months, and the 12-month survival rate was 13 of 48 (27%). On MRI studies, tumor recurrence was absent in seven patients for at least 6 months and for at least 12 months in two patients, one of whom remains recurrence free at more than 24 months. Treatment-characteristic images of injection tracks and intracavity hemoglobin were apparent. In conclusion, the gene therapy is feasible and appears to be satisfactorily safe as an adjuvant to the surgical resection of recurrent GBM, but any benefit appears to be marginal.